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## **Different initial manifestations of the same, rare disease in two newborn infants**

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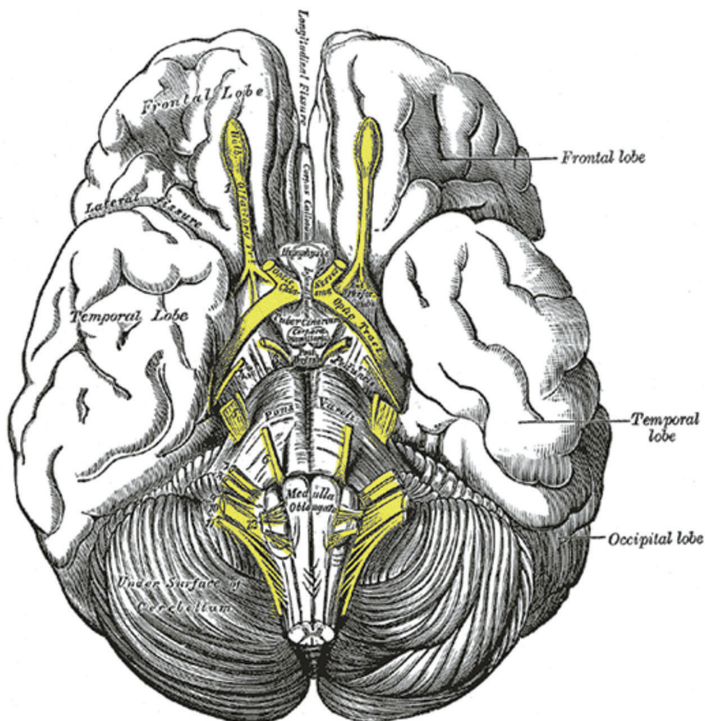
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# Different initial manifestations of the same, rare disease in two newborn infants

June 2014





Hypoglycemia and feeding difficulties are common among infants admitted to neonatal units because of impaired adaptation. In rare cases, however, these are the first signs of an underlying chronic disease. The first case describes a newborn infant that was referred to our tertiary care center because of hypoglycemia and respiratory distress syndrome. Apart from hypoglycemia, the baby displayed feeding difficulties, which could not be fully explained by the respiratory distress. Therefore, a cerebral ultrasound was performed which led to the final diagnosis of a rare disease. The same disease was diagnosed in a late preterm infant, in whom the cerebral ultrasound was performed as a routine examination. We would like to present the different manifestations of a rare underlying disease that was diagnosed in both cases.

## INTRODUCTION

The first patient was born to healthy, non-consanguineous parents at 37 1/7 week of gestation. Except for maternal pyelonephritis during the 32nd week of gestation, the pregnancy had been uneventful. A Caesarean section was performed 46 hours after rupture of membranes due to failure to progress. Apgar scores were 7, 8, and 9 at 1, 5, and 10 minutes, respectively; umbilical arterial cord- pH was 7.28. Birth weight was 2750g (P10-25), length 47 cm (P3-10) and head circumference 34 cm (P25-50). Respiratory distress became apparent in the first minutes of life with tachypnea (respiratory rate of 90/min), interco-

## CASE REPORT 1

stal retractions and intermittent nasal flaring. Supplemental oxygen was provided during the first minutes of life. At the age of 5 hours, the baby seemed to be somnolent. Hypothermia of 35.7 °C and hypoglycemia of 0.5 mmol/l were noted. After oral administration of Maltodextrose, the blood glucose level only rose to 1.5 mmol/l, and the patient was referred to our tertiary care center for further management.

On admission at the age of 8 hours, the patient presented with respiratory distress and an oxygen requirement (FiO<sub>2</sub> 0.25). No dysmorphic signs were noted. In addition to enteral feedings (by nasogastric tube due to poor feeding), an infusion of glucose 10% was provided, and blood glucose levels normalized. On the 4th day of life, parenteral administration of glucose was discontinued. Although respiratory distress had completely resolved by the 3rd day of life, feeding difficulties persisted. A cerebral ultrasound performed on the 4th day of life revealed an absent septum pellucidum (Fig. 1).

MRI of the brain (Fig. 2, 3) confirmed this finding, and, in addition, revealed hypoplasia of the optic nerves, of the optic chiasm and the optical tract, hypoplasia of the genu and rostrum of the corpus callosum, as well as aplasia of the olfactory bulb. The pituitary gland was of low normal volume. Ophthalmological examination confirmed hypoplasia of the optic nerve, and no reaction to light could be observed. Other-

wise, neurological examination was normal. These findings were consistent with a diagnosis of septo-optic dysplasia. The initial feeding difficulties resolved and, at the age of two weeks, the patient gained weight normally with bottle-feeding.

The results of the neonatal screening tests were normal. Since hormonal problems are common in septo-optic dysplasia, a detailed hormonal screening was performed and showed a TSH of 5.86 mU/l (normal range 0.43 - 16.1), fT4 16 pmol/l (normal range 22 - 45), human growth hormone (HGH) 4.4 µg/l (normal range 0.69 - 17.3), cortisol 157 nmol/l (normal range 171 - 537), ACTH 36 ng/l (normal range < 46). Because fT4 concentration was too low for age, our patient was treated with thyroxin 12.5 µg/day from the 8th day of life.

On the 18th day of life, the patient could be discharged home. Neurological examination at the age of 2 months still revealed absent fixation, but was otherwise normal.

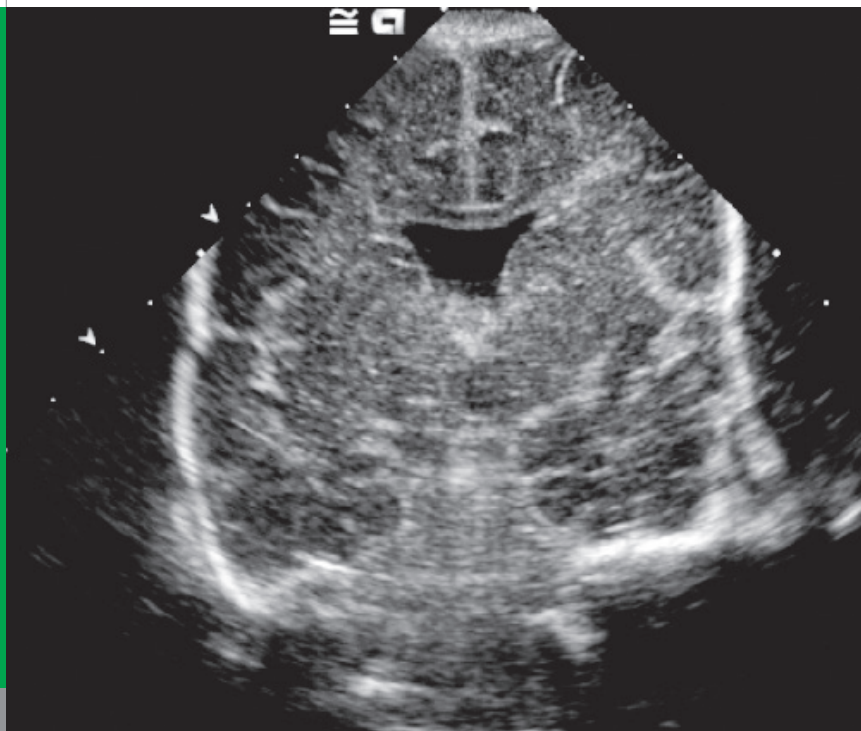


Fig. 1

*Cerebral ultrasound (patient 1): coronal view at the level of foramina of Monro, showing absence of septum pellucidum.*

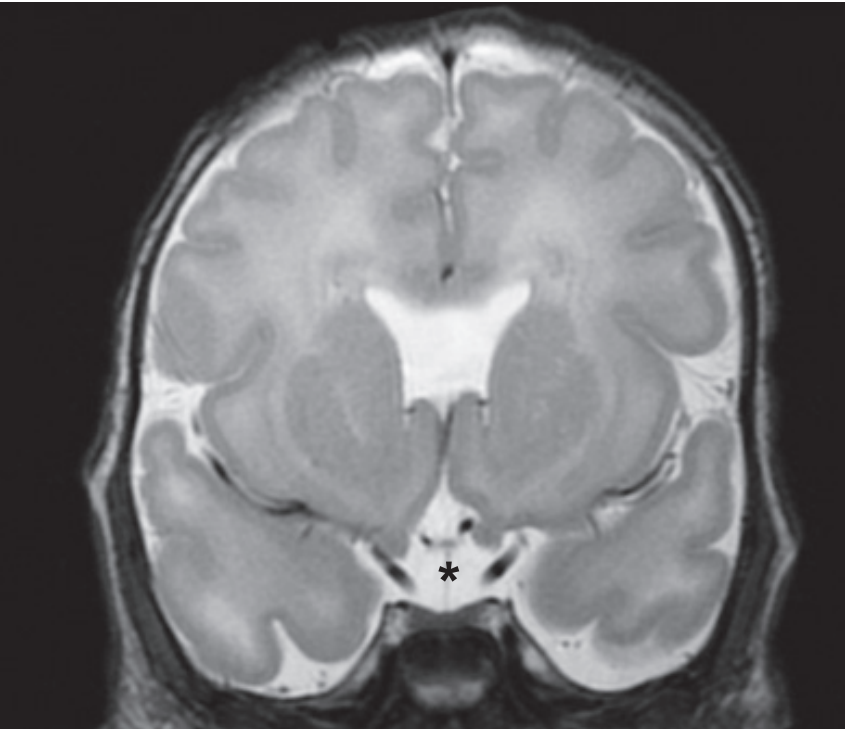
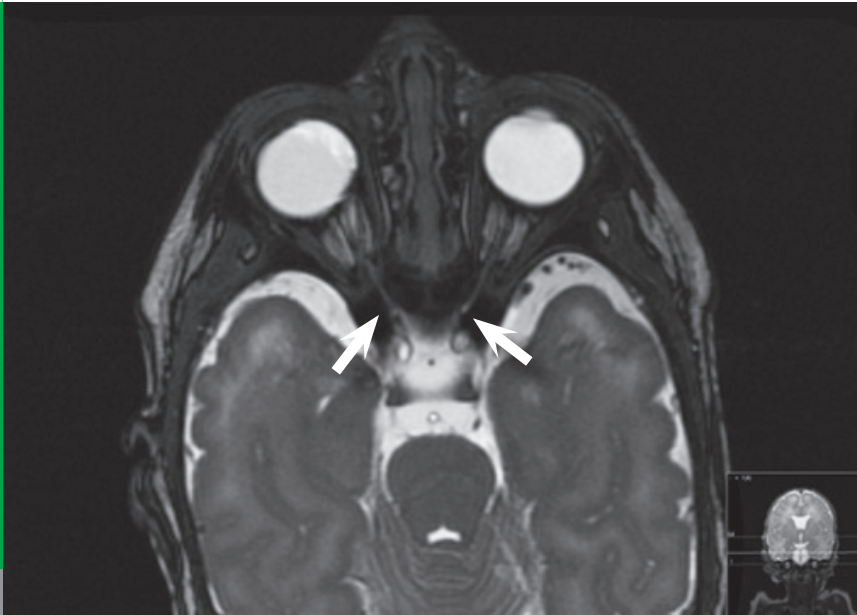


Fig. 2

*MRI T2w TSE (turbo spin sequence, coronal view)  
(patient 1): absent septum pellucidum, hypoplasia of  
the optic chiasm (asterisk).*





**Fig. 3**

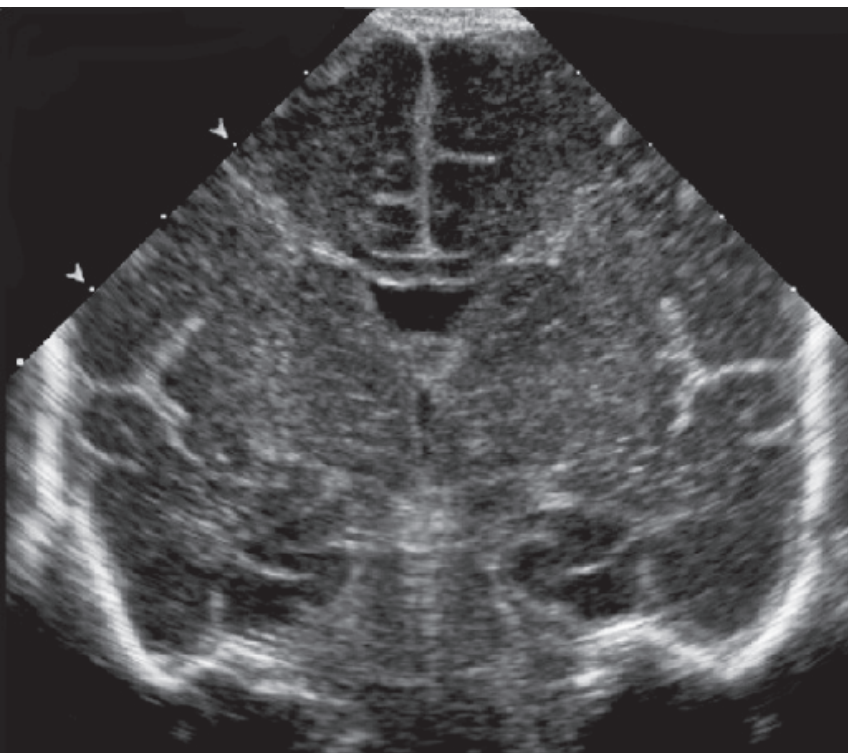
*MRI T2w (3D FIESTA Sequence, axial view) (patient 1):  
hypoplasia of the optic nerves (arrow heads).*

The second patient was born to healthy, non-consanguineous parents at 34 0/7 weeks of gestation. An emergency Caesarean section was performed because of fetal bradycardia and suspected placental abruption. Apgar scores were 7, 8, and 8 at 1, 5, and 10 minutes, respectively, and the umbilical arterial cord-pH was 7.19. Birth weight was 1950 g (P10-25), length 41.5 cm (P3-10) and head circumference 31 cm (P10-25). Because of worsening respiratory distress, the patient was intubated and surfactant was administered on the first day of life. Extubation followed on the 4th postnatal day, and the respiratory symptoms completely resolved by the 9th day of life.

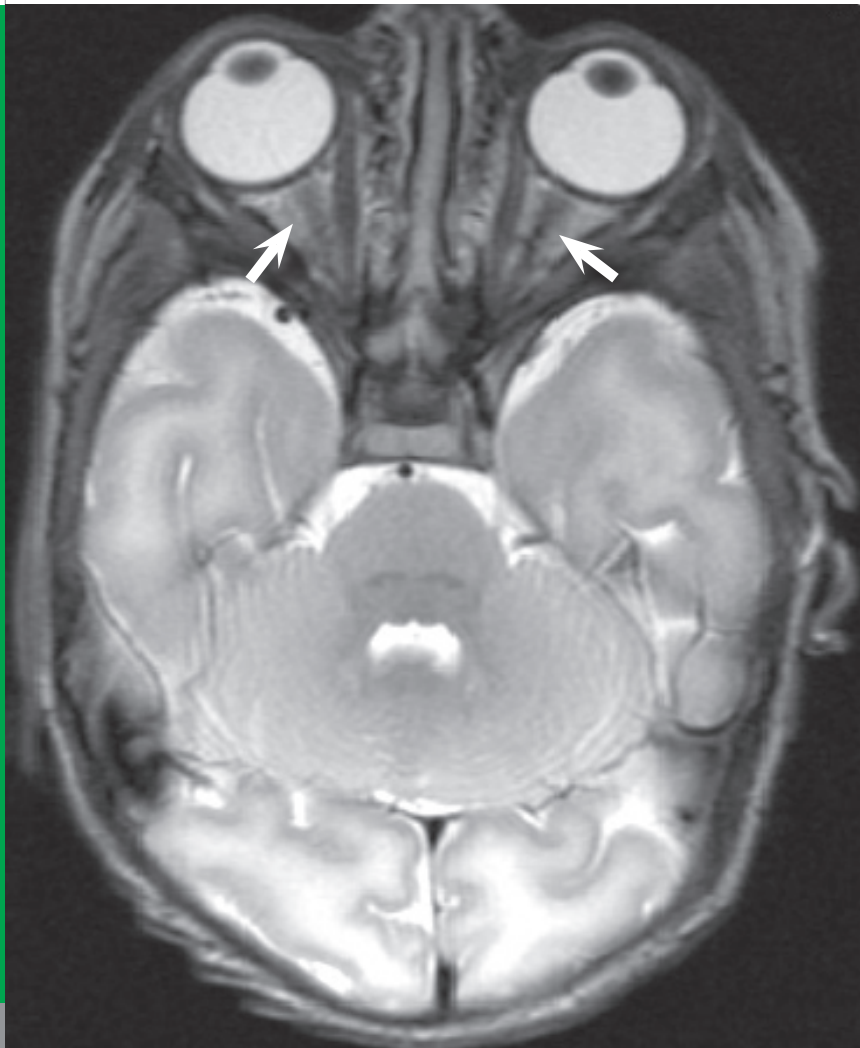
Routine cerebral ultrasound performed on the 1st postnatal day was remarkable for an absent septum pellucidum (Fig. 4). MRI confirmed the absence of the septum pellucidum and demonstrated hypoplasia of the optical nerves, thus establishing the diagnosis of septo-optic dysplasia (Fig. 5, 6). Ophthalmological examination showed severe hypoplasia of the optic nerves, likely to cause severe visual impairment.

The boy developed hypernatremia on the 3rd postnatal day (max. 156 mmol/l), which was initially corrected through increase of fluid supply. Despite increasing fluid intake, hypernatremia and polyuria persisted and were interpreted as a central diabetes insipidus. Therapy with desmopressin was started and the sodium levels normalized. ACTH and cortisol levels were in the

normal range. Because fT4 level was low (12.4 pmol/l) and TSH was normal (1.7mU/l), tertiary hypothyreosis was diagnosed and thyroxin supplementation was started.

**Fig. 4**

*Cerebral ultrasound (patient 2): coronal view at the level of foramina of Monro, showing absence of septum pellucidum.*



**Fig. 5**

*MRI T2w TSE (turbo spin sequence, axial view)  
(Patient 2): hypoplasia of the optic nerves (arrows).*

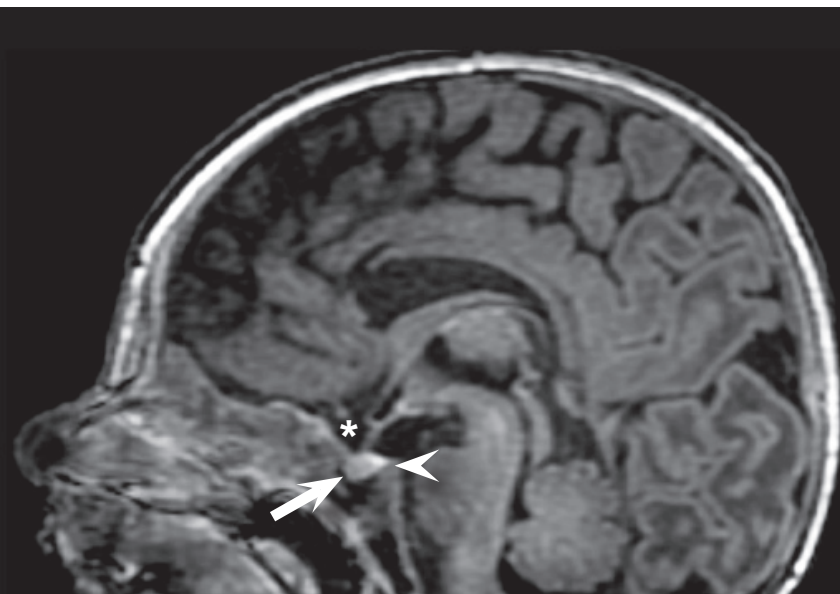


Fig. 6

*MRI T1w 3D (gradient echo sequence, sagittal view) (patient 2): adenohypophysis (arrow), neurohypophysis (arrow head), infundibulum (asterisk).*

## DISCUSSION

Septo-optic dysplasia (SOD) is a condition characterized by the presence of at least two findings of the classical triad that consists of optic nerve hypoplasia or aplasia, pituitary hormone abnormalities and midline brain defects (1). The incidence of SOD is 1:10'000 live births, equally prevalent in males and females (2), and more common in infants born to younger mothers (3). Severity of the clinical manifestations is highly variable. The most commonly reported clinical findings are hypopituitarism (62-80%, mostly human growth hormone deficiency), visual impairment (23%, with significant visual impairment) and developmental delay (3). Developmental delay is more common in children with bilateral (57%) as compared to unilateral (32%) hypoplasia of the optic nerve (3). Early diagnosis is important in order to avoid complications, such as hypoglycemia or hypothyroidism that may further impair neurological development.

Although SOD is usually diagnosed beyond the neonatal period, these two cases show that the diagnosis can also be made in newborn infants. Clinically, SOD should be suspected in newborns with unexplained or persistent hypoglycemia, jaundice, nystagmus or midline defects. Because early diagnosis may be associated with a better outcome, SOD must be considered in newborn infants who present with these clinical symptoms.

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